

Sleep-related melatonin use in healthy children

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Abstract

Question A mother brought her 12-year-old son into my office because she is concerned that he has difficulty falling asleep almost every night. Her job involves shift work and she uses melatonin herself to help her fall asleep. She asked if her son could take melatonin. What are the recommendations and considerations for using melatonin in otherwise healthy children and adolescents?

Answer Insomnia is reported in up to a quarter of healthy children and in three-quarters of children with neurodevelopmental and psychiatric conditions, resulting in negative consequences. For children with delayed sleep phase syndrome, melatonin can be a useful treatment together with insomnia evaluation and regular follow-up. For children with otherwise undiagnosed insomnia and healthy sleep hygiene, melatonin use should be considered. While melatonin seems to be safe, there is a lack of evidence for its routine use among healthy children.



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Up to 25% of healthy children and adolescents, as well as up to 75% of children with neurodevelopmental or psychiatric conditions, experience difficulty with sleep.^{1,2} Studies continue to demonstrate both short-term and long-term negative consequences of poor sleep in children, including poor concentration, hyperactivity, irritability, poor memory, anxiety, depression, driving safety issues, learning difficulties, and poorer school and daytime performance.^{2,3}

Insomnia in children

Considerable variability exists in children's sleep duration.⁴ A 16-year longitudinal study from Zurich, Switzerland, which followed parental-reported sleep duration of nearly 500 children, provided the basis for standardized percentile curves of sleep duration, serving as a guide for parental expectations.⁵

Pediatric insomnia is defined as repeated difficulty with sleep initiation, duration, consolidation, or quality that occurs despite age-appropriate time and opportunity for sleep, leading to daytime functional impairment for the child and family.² Several conditions can lead to pediatric insomnia with 2 of the most common being delayed sleep phase syndrome (DSPS) and behavioural insomnia of childhood.^{6,7}

In an infant with normal growth and development, an organic cause of insomnia is unlikely, and behavioural or feeding-related issues should be assessed.⁷ In some infants, gastroesophageal reflux might be the cause of interrupted or delayed sleep.⁷

In toddlers, sleep disturbances are most commonly associated with fears, and behavioural interventions such as

graduated extinction, parental education, and appropriate bedtime routines have been demonstrated to be effective.^{6,7}

In adolescents, DSPS is the most common cause of insomnia.⁷ The child will fall asleep later than expected and have difficulty waking up the next morning as the internal circadian pacemaker is not synchronized with the child's environmental time. Improved sleep hygiene with the addition of melatonin can be useful.³

Melatonin

Sleep hygiene is key to resolving behaviour-related causes of insomnia. **Box 1** presents sleep hygiene recommendations for children.^{2,6} Melatonin is becoming

Box 1. Recommendations for good sleep hygiene for children

- Napping during the day should be avoided
- Appropriate dinnertime should be at least 2 hours before bedtime
- Screen time (ie, watching television, playing computer or video games) should be discontinued at least an hour before bedtime
- Regular bedtime routine including routine sleep and wake-up times should be maintained
- Children should sleep in their own beds
- Sleep environment should be dark and quiet; room should not be too hot
- Caffeine, nicotine, and alcohol should be avoided

Data from Mindell et al² and Owens and Moturi.⁶

a popular choice for management among parents and practitioners, despite the absence of any specific pediatric guidelines.^{2,8}

Melatonin is a hormone naturally synthesized by the pineal gland, and its secretion is regulated by the suprachiasmatic nucleus in the hypothalamus.^{3,6} Starting at 3 months of age, high levels of melatonin are secreted at night and low levels are secreted during the day.⁹ The circadian pattern of melatonin secretion is the essential mechanism of the sleep-wake cycle.^{6,9} Melatonin has a chronobiotic effect, or circadian phase-shifting effect, and a less established hypnotic and sleep-promoting effect.⁶ With a half-life of 40 minutes, and extensive first-pass metabolism, melatonin will reach its peak concentration within 1 hour of administration.⁶ Health Canada considers melatonin a natural health product, and it is available in many unique products in Canada.¹⁰ Neither Health Canada nor the US Food and Drug Administration approve melatonin for sleep disorders in children and adolescents, thus its use in children is considered "off-label."^{6,8}

Effectiveness

There are conflicting reports in the literature on the effectiveness of melatonin for sleep, and this is attributed to subject diversity and differences in dosage, timing, and study designs.⁷ In a double-blind, placebo-controlled trial with 40 children aged 6 to 12, Smits and colleagues confirmed sleep onset with an actigraph. Children received placebo or 5 mg of fast-release melatonin at 6 PM for a period of 4 weeks after establishing a 1-week baseline. The treatment group fell asleep earlier (9:09 PM and 10:06 PM for the melatonin group and placebo group, respectively; $P=.005$) with increased total sleep (9 hours and 43 minutes and 9 hours and 14 minutes for the melatonin group and placebo group, respectively; $P=.026$).¹¹ Although 11 of these children were taking methylphenidate for attention deficit hyperactivity disorder, covariance analysis found melatonin to be just as effective.¹¹

Because of its immunomodulating properties, melatonin is contraindicated in those with immune and lymphoproliferative disorders, as well as in those taking immunosuppressants.^{6,12} Some experts and a few small studies present conflicting findings suggesting that melatonin either lowers or increases seizure thresholds.⁶ Very limited data show that it suppresses the hypothalamic-pituitary-gonadal axis, as endogenous levels of melatonin were found to be elevated in 7 male patients with gonadotropin-releasing hormone deficiency.¹³

Following failure of behaviour modifications, as well as ruling out any other medical causes of insomnia, trying pharmacologic treatment with melatonin seems appropriate. No clear dosing guidelines exist, with effective doses varying across studies. The Canadian Paediatric Society recommends 1 mg of melatonin in

infants, 2.5 to 3 mg in older children, and 5 mg in adolescents.⁸ The range in children with special needs varies from 0.5 to 10 mg.^{7,14} Melatonin should be given 30 to 60 minutes before bedtime.⁸

Of interest, termination of melatonin might result in phase shift if no behaviour changes are implemented.³ Practitioners should ensure that children have regular follow-up to reevaluate insomnia and determine if melatonin should be continued.

Safety profile

With only small studies, most focusing on children with neurodevelopmental abnormalities, further randomized studies of the pharmacokinetics and pharmacodynamics of melatonin in otherwise healthy children are needed.^{2,8} Among a cohort of 101 children from the Netherlands between the ages of 6 and 12 with attention deficit hyperactivity disorder and DSPS who took melatonin for 4 weeks (3 mg for children who weighed 40 kg or less and 6 mg for those who weighed 40 kg or more), 65% of the children continued to use melatonin daily 3.7 years later, and their parents reported no concerns or adverse side effects.¹⁵

Conclusion

Expert panels agree that for circadian rhythm disorders, specifically for DSPS, melatonin can be prescribed with regular follow-up and insomnia evaluation. For children with insomnia who have unremarkable medical histories and physical examination findings and who practise good sleep hygiene, melatonin might be an appropriate treatment to try; however, no clear endorsement can be found in available protocols. The long-term safety profile for melatonin in otherwise healthy children has yet to be established. While melatonin does appear to be well tolerated, it should be avoided in children with immune disorders or those using immunomodulating treatments. 🌿

Competing interests

None declared

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